## REMARKS

Claim 1 has been amended. As a result, Claims 1-6 remain pending in the present application. Support for the amendments can be found in the specification and claims as filed. Accordingly, the amendments do not constitute the addition of new matter. Reconsideration of the application in view of the foregoing amendments and following comments is respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected Claims 1-6 under 35 U.S.C. § 112, first paragraph. According to the Examiner, the specification, while being enabling for a method of detecting antibodies against certain autoantigens and for indicating the presence or possibility of cardiovascular disease, does not reasonably provide enablement for a method of diagnosing the severity of cardiovascular disease, nor for prediction of early pathogenic reaction for cardiovascular disease. As amended, Claim 1 recites, *inter alia*, "[a] method for diagnosing an ongoing pathology or predicting early pathogenic reaction for cardiovascular disease." Accordingly, the specification is enabling for Claim 1.

The Examiner further rejected Claims 1 and 3-6 under 35 U.S.C. § 112, first paragraph, because the Examiner believes that the specification is not enabling for a method of detecting antibodies against any and all autoantigens. As amended, Claim 1 recites, *inter alia*, "determining a level of antibodies, wherein said antibodies are able to bind to an autoantigen or a corresponding recombinant antigen or synthetic peptide for cardiovascular disease in a saliva sample from said patient." In Claim 1, the autoantigens are for cardiovascular disease, which is stated in the claim and supported by the disclosure. The specification provides enablement for Claim 1 with regard to the autoantigens for cardiovascular disease, as indicated in the Examples on pages 13-22. Several autoantigens were tested with regard to cardiovascular disease, including myosin, oxidized LDL, β-2-glycoprotein-1, and heat shock protein-60. With a number of examples of autoantigens for cardiovascular disease, the specification is enabling for Claim 1.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected Claims 1-6 under 35 U.S.C. § 112, second paragraph. According to the Examiner, Claim 1 is confusing because the preamble of the claim does not correlate with the analysis of the detected result. As amended, Claim 1 recites, *inter alia*, "[a] method for diagnosing an ongoing pathology or predicting early pathogenic reaction for cardiovascular disease." Accordingly, the preamble of the claim correlates with the analysis of the detected result.

The Examiner also believes that Claim 1 is vague and indefinite because it recites a method for diagnosing the likelihood of cardiovascular disease in a patient using a sample from the patient. In particular, the Examiner states that Claim 1 recites a method involving the determination of antibodies against a recombinant antigen or synthetic peptide in a sample and that recombinant antigens and synthetic peptides are not generally present in a patient sample. The Examiner states that, therefore, it is unclear how antibodies may exist against such antigens.

As amended, Claim 1 recites, *inter alia*, "determining a level of antibodies, wherein said antibodies are able to bind to an autoantigen or a corresponding recombinant antigen or synthetic peptide for cardiovascular disease in a saliva sample from said patient."

Support for the amendment can be found in Paragraph [0049] of the specification which states, "[t]he test utilizes a highly sensitive and accurate ELISA test method that measures saliva IgA specific antibody titers to the purified antigens or a corresponding recombinant antigen or synthetic peptide from autoantigens." The antibodies are measured from the patient sample. These antibodies can be raised against an autoantigen or a corresponding recombinant or synthetic peptide. In particular, these antibodies can bind to the autoantigens or corresponding recombinant or synthetic peptides that have been bound to a plate for an assay. Accordingly, the recombinant and synthetic peptides are not necessarily present in the patient sample. The

examples of the specification further support Claim 1 by showing that the autoantigens or corresponding recombinant or synthetic peptides are bound to the microtiter plate for antibody binding assays.

According to the Examiner, Claim 2 is vague and indefinite because it is unclear as to the type of immune complexes that are being detected or how these unknown complexes can be correlated to cardiovascular disease. Paragraph [0024] of the specification discloses that "[i]mmune complexes are formed when antigens bind to antibodies. Antigen-antibody complexes can activate the complement cascade and bind to the C1q component of complement and form pathologic complexes." Accordingly, the term "immune complexes" in Claim 2 is clearly defined in the specification.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejections under 35 U.S.C. § 112, second paragraph.

Double Patenting

The Examiner rejected Claims 1-6 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-8 of co-pending application Serial No. 10/005,682 (Our Reference No.: IMSCI2.005A). A Terminal Disclaimer in accordance with 37 C.F.R. § 1.321(c) is filed herewith. Accordingly, Applicant respectfully requests the Examiner to withdraw the rejection under the judicially created doctrine of obviousness-type double patenting.

Rejection under 35 U.S.C. § 102

The Examiner rejected Claims 1-4 under 35 U.S.C. § 102(b) as being anticipated by Kovanen et al. (Archives of Internal Medicine, July 13, 1998. Vol.158, No. 13, pgs. 1434-1439). Kovanen et al. discloses elevated levels of IgA, IgE, and IgG in patients with established arteriosclerosis and myocardial infarction or cardiac death. Kovanen et al. also discloses autoantigens and several exogenous antigens as having been implicated in the pathogenesis of myocardial infarction including oxidized LDL and cardiolipin.

According to M.P.E.P. 2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

As amended, Claim 1 recites, *inter alia*, "determining a level of antibodies, wherein said antibodies are able to bind to an autoantigen or a corresponding recombinant antigen or synthetic peptide for cardiovascular disease in a saliva sample from said patient."

Accordingly, Kovanen et al. does not anticipate Claim 1 because it does not disclose that levels of IgA, IgE, and IgG can be measured with saliva samples. In Kovanen et al., on page 1434 in the methods section, serum samples were used for study. The introduction section of Kovanen et al. on pages 1434-1435 makes a strong correlation between the testing of serum and levels of antibodies associated with atherosclerosis. Accordingly, Kovanen et al. does not disclose the use of saliva for measuring levels of IgA, IgE, and IgG. Therefore, Kovanen et al. does not disclose each and every element as set forth in the claim.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 102(b).

Rejection under 35 U.S.C. § 103

The Examiner also rejected Claims 5 and 6 under 35 U.S.C. § 103(a) as being unpatentable over Kovanen et al. in view of Stone et al. (Journal of Human Stress, 1987, Vol. 13, pg. 136-140).

According to M.P.E.P. 2143.03, "[o]bviousness can only be established by combining or modifying the teaching of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the references themselves or in the knowledge generally available to one of ordinary skill in the art."

As stated above, the introduction section of Kovanen et al. on pages 1434-1435 makes a strong correlation between the testing of serum and levels of antibodies associated with atherosclerosis. On page 1435, Kovanen et al. "investigated the association between the levels of serum immunoglobulin classes A, E, G, and M and myocardial infarction or cardiac death" alone

(emphasis added). In the rest of its introduction, Kovanen et al. elaborates on serum samples. Kovanen et al. does not teach or suggest the use of saliva for measuring levels of IgA, IgE, and IgG.

While Stone et al. teaches the measurement of IgA antibody response to a particular antigen in saliva using ELISA to study immunocompetence, Stone et al. does not suggest using saliva samples to test for autoantigen. Indeed, on page 138-139, Stone et al. discloses that the measurement of secretory IgA is directed to exposure to environmental antigens, viruses, and bacteria. Stone et al. does not teach or suggest that the same effect can be seen with autoantigens. In fact, Stone et al. presents the secretory IgA as related to environmental factors. See, for instance, page 136 of Stone et al. which discloses that secretory IgA "binds to invading organisms more effectively than the form of IgA in serum" and suggests that measurement of secretory IgA will be used in response to the "importance in prevention of infectious disease." Furthermore, Stone et al. discloses that "[a]lthough IgA is also present in the serum, secretory IgA (s-IgA) is very different from serum immunoglobulin." In view of these teachings, there is no motivation to combine Stone et al. with Kovanen et al. to create the claimed invention. Such a motivation is necessary to create a *prima facie* showing of obviousness.

Moreover, even if there were motivation to combine the references, there would be no reasonable expectation of success in creating the claimed invention. According to M.P.E.P.2143.02, "[o]bviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness." Stone et al. discloses that secretory IgA is different from serum IgA and that saliva testing for secretory IgA can be used for exposure to environmental antigens, such as viruses and bacteria. One skilled in the art would have no expectation that testing saliva could be used as a reliable test for autoantigens, as presently claimed. Accordingly, combining the Stone et al. disclosure with Kovanen et al. would not produce the reasonable expectation of success required to produce a *prima facie* showing of obviousness.

Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 103(a).

## CONCLUSION

In view of the foregoing amendments and comments, it is respectfully submitted that the present application is fully in condition for allowance, and such action is earnestly solicited.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully invited to call the undersigned in order to resolve such issue promptly.

Respectfully submitted,

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Dated: August 25, 2004

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